

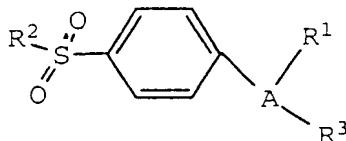
What is claimed is :

1. A combination comprising a therapeutically-effective amount of a cyclooxygenase-2 inhibitor, a
 5 leukotriene B₄ receptor antagonist and an immunosuppressive drug, wherein the immunosuppressive drug is selected from the group consisting of antiproliferative agents, antiinflammatory-acting compounds and inhibitors of leukocyte activation.

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2. The combination of Claim 1 wherein the cyclooxygenase-2 inhibitor is selected from Dupont Dup-697, Taisho NS-398, meloxicam, flosulide or compounds of Formula I

15

**I**

wherein:

A is a 5- or 6-member ring substituent selected
 20 from partially unsaturated or unsaturated heterocyclo or carbocyclic rings;

R¹ is at least one substituent selected from the group consisting of heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally
 25 substituted at a substitutable position with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

R² is selected from the group consisting of alkyl, and amino; and

R³ is a radical selected from the group consisting of halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo,

cycloalkenyl, aralkyl, heterocycloalkyl, acyl,
alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl,
arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl,
arylthioalkyl, aryloxyalkyl, aralkylthioalkyl,
5 aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl,
aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl,
N-arylamino, N-arylamino, N-alkyl-N-arylamino,
alkylaminocarbonyl, carboxyalkyl, alkylamino, N-
arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-
10 alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-
arylaminoalkyl, N-aralkylaminoalkyl, N-alkyl-N-
aralkylaminoalkyl, N-alkyl-N-arylaminoalkyl, aryloxy,
aralkoxy, arylthio, aralkylthio, alkylsulfinyl,
alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-
15 arylaminosulfonyl, arylsulfonyl, and N-alkyl-N-
arylaminoalkyl;
or a pharmaceutically-acceptable salt thereof.

3. The combination of Claim 1 wherein the
20 leukotriene B₄ receptor antagonist is selected from the
group consisting of calcitriol, ontazolast, Bayer Bay-x-
1005, Ciba-Geigy CGS-25019C, ebselen, Leo Denmark ETH-
615, Lilly LY-293111, Ono ONO-4057, Terumo TMK-688,
Boehringer Ingelheim BI-RM-270, Lilly LY 213024, Lilly
25 LY 264086, Lilly LY 292728, Ono ONO LB457, Pfizer
105696, Perdue Frederick PF 10042, Rhone-Poulenc Rorer
RP 66153, SmithKline Beecham SB-201146, SmithKline
Beecham SB-201993, SmithKline Beecham SB-209247, Searle
SC-53228, Shionogi S-2472, Searle SC-52798, Leo Denmark
30 SR-2566, Tanabe T-757, Sumitomo SM 15178, and American
Home Products WAY 121006.

4. The combination of Claim 3 wherein the
leukotriene B₄ receptor antagonist is selected from the
35 group consisting of calcitriol, ontazolast, Bayer Bay-x-
1005, Ciba-Geigy CGS-25019C, ebselen, Leo Denmark ETH-
615, Lilly LY-293111, Ono ONO-4057, SmithKline Beecham
SB-201993, SmithKline Beecham SB-209247, Warner-Lambert

BPC-15, Pfizer 105696, Shionogi S-2472, Searle SC-52798,
Leo Denmark SR-2566, Tanabe T-757, and Terumo TMK-688.

5 5. The combination of Claim 2 wherein the
cyclooxygenase-2 inhibitor is selected from compounds of
Formula I.

10 6. The combination of Claim 5 wherein A is selected
from the group consisting of oxazolyl, isoxazolyl,
thienyl, dihydrofuryl, furyl, pyrrolyl, pyrazolyl,
thiazolyl, imidazolyl, isothiazolyl, cyclopentenyl,
phenyl, and pyridyl; wherein R¹ is selected from the
group consisting of 5- and 6-membered heterocyclo, lower
cycloalkyl, lower cycloalkenyl and aryl, wherein the
15 aryl is selected from the group consisting of phenyl,
biphenyl and naphthyl, wherein R¹ is optionally
substituted at a substitutable position with one or more
radicals selected from the group consisting of lower
alkyl, lower haloalkyl, cyano, carboxyl, lower
20 alkoxycarbonyl, hydroxyl, lower hydroxyalkyl, lower
haloalkoxy, amino, lower alkylamino, phenylamino, nitro,
lower alkoxyalkyl, lower alkylsulfinyl, halo, lower
alkoxy and lower alkylthio; wherein R² is selected from
the group consisting of lower alkyl and amino; and
25 wherein R³ is a radical selected from the group
consisting of halo, lower alkyl, oxo, cyano, carboxyl,
lower cyanoalkyl, heteroaryloxy, lower alkyloxy, lower
cycloalkyl, phenyl, lower haloalkyl, 5- or 6-membered
heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl,
30 phenylcarbonyl, lower alkoxyalkyl, heteroaryloxy,
alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl,
alkylamino, aminoalkyl, alkylaminoalkyl, aryloxy, and
aralkoxy; or a pharmaceutically-acceptable salt thereof.

35 7. The combination of Claim 6 wherein A is
selected from the group consisting of oxazolyl,
isoxazolyl, dihydrofuryl, imidazolyl, and pyrazolyl;
wherein R¹ is selected from the group consisting of 5-

and 6-membered heterocyclo, and aryl, wherein aryl is selected from the group consisting of phenyl, biphenyl and naphthyl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals

5 selected from the group consisting of lower alkyl, lower haloalkyl, cyano, carboxyl, lower alkoxy carbonyl, hydroxyl, lower hydroxyalkyl, lower haloalkoxy, amino, lower alkylamino, phenylamino, nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy and lower
10 alkylthio; wherein R² is amino; and wherein R³ is a radical selected from the group consisting of oxo, cyano, carboxyl, lower alkoxy carbonyl, lower carboxyalkyl, lower cyanoalkyl, halo, lower alkyl, lower alkyl oxy, lower cycloalkyl, phenyl, lower haloalkyl, 5-
15 or 6-membered heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl, phenylcarbonyl, lower alkoxyalkyl, 5- or 6-membered heteroaryloxy, aminocarbonyl, lower alkylaminocarbonyl, lower alkylamino, lower aminoalkyl, lower alkylaminoalkyl, phenoxy, and lower aralkoxy; or
20 a pharmaceutically-acceptable salt thereof.

8. The combination of Claim 7 wherein A is selected from the group consisting of oxazolyl, isoxazolyl, imidazolyl, and pyrazolyl; wherein R¹ is phenyl optionally substituted at a substitutable position with one or more radicals selected from the group consisting of methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, trifluoromethyl, cyano, carboxyl, methoxycarbonyl, hydroxyl, hydroxymethyl, trifluoromethoxy, amino, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, nitro, methoxymethyl, methylsulfinyl, fluoro, chloro, bromo, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, and methylthio; wherein R² is amino; and wherein R³ is a radical selected from the group consisting of oxo, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, carboxypropyl, carboxymethyl, carboxyethyl, cyanomethyl, fluoro,

chloro, bromo, methyl, ethyl, isopropyl, butyl, *tert*-butyl, isobutyl, pentyl, hexyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl,
5 heptafluoropropyl, fluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, cyclohexyl, phenyl, pyridyl, thienyl, thiazolyl, oxazolyl, furyl, pyrazinyl, hydroxymethyl, hydroxylpropyl, benzyl, formyl,
10 phenylcarbonyl, methoxymethyl, furylmethoxy, aminocarbonyl, N-methylaminocarbonyl, N,N-dimethylaminocarbonyl, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, aminomethyl, N,N-dimethylaminomethyl, N-methyl-N-ethylaminomethyl, benzyloxy, and phenoxy; or a
15 pharmaceutically-acceptable salt thereof.

9. The combination of Claim 8 wherein the cyclooxygenase-2 inhibitor is selected from compounds, their prodrugs and their pharmaceutically-acceptable salts, of the group consisting of

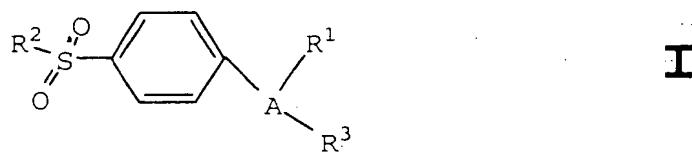
3-(3,4-difluorophenyl)-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;
25 3-phenyl-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
30 4-[5-(3-fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
3-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-1H-imidazol-2-yl]pyridine;
2-methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-
35 trifluoromethyl-1H-imidazol-2-yl]pyridine;
4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide;
4-[5-methyl-3-phenylisoxazol-4-yl]benzenesulfonamide;

4-[5-hydroxyethyl-3-phenylisoxazol-4-yl]benzenesulfonamide;
[2-trifluoromethyl-5-(3,4-difluorophenyl)-4-oxazolyl]benzenesulfonamide;
5 4-[2-methyl-4-phenyl-5-oxazolyl]benzenesulfonamide; and
4-[5-(3-fluoro-4-methoxyphenyl-2-trifluoromethyl)-4-oxazolyl]benzenesulfonamide.

10. The composition of Claim 1 wherein the
leukocyte activation inhibitor is a cyclosporin.

11. The composition of Claim 10 wherein the cyclosporin is cyclosporin A.

15 12. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a therapeutically-effective amount of a leukotriene B₄ receptor antagonist, a cyclosporin and a cyclooxygenase-2 inhibitor selected from Dupont Dup 697, Taisho NS-398,
20 meloxicam, flosulide or compounds of Formula I



wherein:

25 A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo or carbocyclic rings;

30 R¹ is at least one substituent selected from the group consisting of heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

R² is selected from the group consisting of alkyl, and amino; and

R³ is a radical selected from the group consisting of halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, 5 cyanoalkyl, heterocyclooxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, 10 arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N- 15 arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-aryl amino, aminoalkyl, alkylaminoalkyl, N-aryl aminoalkyl, N-aralkylaminoalkyl, N-alkyl-N- aralkylaminoalkyl, N-alkyl-N-aryl aminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, 20 alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, and N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

25 13. The combination of Claim 12 wherein the cyclooxygenase-2 inhibitor is selected from compounds of Formula I.